

## IN THE SPECIFICATION

Bracketed language is present in the original.

(1) Delete the paragraph at page 3, line 22, to page 4, line 15 and insert:

05  
A sequence which has at least 75% identity to SEQ ID NO:155 (e.g. 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity); or a sequence which has at least 50% identity to SEQ ID NO:155 (e.g. 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, 60%, 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 115, 120, 125, 130, 135, 140, 145, etc., contiguous nucleotides) of SEQ ID NO:155; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 115, 120, 125, 130, 135, 140, 145, etc., contiguous nucleotides) of SEQ ID NO:155 and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level. This sequence will typically be at the 5' end of the RNA. SEQ ID NO:155 is the nucleotide sequence of the start of R region in the LTR of the 'ERVK6' HML-2 virus [ref. 1]. This portion of the R region is found in all full-length HML-2 transcripts.

(2) Delete the paragraph at page 4, line 16, to page 5, line 9 and insert:

06  
A downstream region comprising a sequence which has at least 75% sequence identity to SEQ ID NO:156 (e.g. 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity);

Ab cont.

or a sequence which has at least 50% identity to SEQ ID NO:156 (e.g. 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, 60%, 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, etc., contiguous nucleotides) of SEQ ID NO:156; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, etc., contiguous nucleotides) of SEQ ID NO:156 and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level. SEQ ID NO:156 is the nucleotide sequence of the RU5 region downstream of SEQ ID NO:155 in the ERVK6 LTR. This region is found in full-length HML-2 transcripts, but may not be present in all mRNAs transcribed from a HML-2 LTR promoter.

(3) Delete the paragraph at page 5, lines 10-31 and insert:

A7

A downstream region comprising a sequence which has at least 75% sequence identity to SEQ ID NO:6 (e.g. 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity); or a sequence which has at least 50% identity to SEQ ID NO:6 (e.g. 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, 60%, 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100%

Q1 identity) and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, etc., contiguous nucleotides) of SEQ ID NO:6; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, etc., contiguous nucleotides) of SEQ ID NO:6 and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level. SEQ ID NO:6 is the nucleotide sequence of the region of the ERVK6 virus between the U5 region and the first 5' splice site. This region is found in full-length HML-2 transcripts, but has been lost by some variants and, like region 2 above, may not be present in all mRNAs transcribed from a HML-2 LTR promoter.

---

(4) Delete the paragraph at page 6, lines 6-31 and insert:

---

Q8 A downstream region comprising a sequence which has at least 75% sequence identity to SEQ ID NO:5 (e.g. 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity); or a sequence which has at least 50% identity to SEQ ID NO:5 (e.g. 51%, 52%, 53%, 54%, 55%, 56%, 57%, 58%, 59%, 60%, 61%, 62%, 63%, 64%, 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280,

285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, etc., contiguous nucleotides) of SEQ ID NO:5; or a sequence which has at least 80% identity (e.g. 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, 99.5%, 99.9%, 100% identity) to at least a 20 contiguous nucleotide fragment (e.g. . 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 115, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 290, 295, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, etc., contiguous nucleotides) of SEQ ID NO:5 and is expressed at least 1.5 fold (e.g. 2, 2.5, 5, 10, 20, 50, etc., fold) higher level relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level. SEQ ID NO:5 is the nucleotide sequence of the U3R region in the 3' end of ERVK6. This sequence will typically be near the 3' end of the RNA, immediately preceding any polyA tail.

(5) Delete the paragraph at page 7, line18, to page 8, line 20 and insert:

In general, therefore, the mRNA to be detected has the formula  $N_1-N_2-N_3-N_4-N_5$ -polyA, wherein:

— N1 has at least 75% sequence identity to SEQ ID NO:155; or has at least 50% identity to SEQ ID NO:155 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:155; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:155 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level;

— N2 has at least 75% sequence identity to SEQ ID NO:156; or has at least 50% identity to SEQ ID NO:156 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:156; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:156 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level;

— N3 has at least 75% sequence identity to SEQ ID NO:6; or has at least 50% identity to SEQ ID NO:6 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:6; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:6 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level;

— N4 comprises any RNA sequence;

— N5 has at least 75% sequence identity to SEQ ID NO:5; or has at least 50% identity to SEQ ID NO:5 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:5; or has at least 80% identity to at least a 20 contiguous nucleotide fragment of SEQ ID NO:5 and is expressed at least 1.5 fold higher relative to expression in a normal (i.e., non cancerous) cell with at least a 95% confidence level; and

— at least one of N<sub>1</sub>, N<sub>2</sub>, N<sub>3</sub>, N<sub>4</sub> or N<sub>5</sub> is present, but polyA is optional.

(6) Delete the paragraph at page 9, lines 5-12 and insert:

Where diagnosis is based on mRNA detection, the method of the invention preferably comprises an initial step of: (a) extracting RNA (e.g. mRNA) from a patient sample; (b) removing DNA from a patient sample without removing mRNA; and/or (c) removing or disrupting DNA which comprises SEQ ID NO:4, but not RNA which comprises SEQ ID NO:4, from a patient sample. This is necessary because the genomes of both normal and cancerous prostate cells contain multiple PCAV DNA templates, whereas increased PCA-mRNA levels are only found in cancerous cells. As an alternative, a RNA-specific assay can be used which is not affected by the presence of homologous DNA.

(7) Delete the paragraph at page 9, lines 18-21 and insert:

Methods for removing DNA, but not RNA, comprising PCA-mRNA sequences will use a reagent which is specific to a sequence within a PCA-mRNA e.g. a restriction enzyme which recognizes a DNA sequence within SEQ ID NO:4, but which does not cleave the corresponding

*all* RNA sequence.

(8) Delete the paragraph at page 16, lines 7-9 and insert:

*Q12* Examples of gag nucleotide sequences are: SEQ ID NOS:7, 8, 9 & 11 [HERV-K(CH)];  
SEQ ID NO:85 [HERV-K108]; SEQ ID NO:91 [HERV-K(C7)]; SEQ ID NO:97 [HERV-K(II)];  
SEQ ID NO:102 [HERV-K10].

(9) Delete the paragraph at page 16, lines 10-12 and insert:

*Q13* Examples of gag polypeptide sequences are: SEQ ID NOS:46, 47, 48, 49, 56 & 57  
[HERV-K(CH)]; SEQ ID NO:92 [HERV-K(C7)]; SEQ ID NO:98 [HERV-K(II)]; SEQ ID  
NOS:103 & 104 [HERV-K10]; SEQ ID NO:146 ['ERV6'].

(10) Delete the paragraph at page 16, lines 17-18 and insert:

*Q14* Examples of prt nucleotide sequences are: SEQ ID NO:86 [HERV-K(108)]; SEQ ID  
NO:99 [HERV-K(II)]; SEQ ID NO:105 [HERV-K10].

(11) Delete the paragraph at page 16, lines 19-20 and insert:

*Q15* Examples of prt polypeptide sequences are: SEQ ID NO:106 [HERV-K10]; SEQ ID  
NO:147 ['ERV6'].

(12) Delete the paragraph at page 16, lines 24-25 and insert:

*Q16* Examples of pol nucleotide sequences are: SEQ ID NO:87 [HERV-K(108)]; SEQ ID  
NO:93 [HERV-K(C7)]; SEQ ID NO:100 [HERV-K(II)]; SEQ ID NO:107 [HERV-K10].

(13) Delete the paragraph at page 16, lines 26-27 and insert:

*Q17* Examples of pol polypeptide sequences are: SEQ ID NO:94 [HERV-K(C7)]; SEQ ID  
NO:108 [HERV-K10]; SEQ ID NO:148 ['ERV6'].

(14) Delete the paragraph at page 17, lines 4-5 and insert:

*Q18* Examples of env nucleotide sequences are: SEQ ID NO:88 [HERV-K(108)]; SEQ ID  
NO:95 [HERV-K(C7)]; SEQ ID NO:101 [HERV-K(II)]; SEQ ID NO:107 [HERV-K10].

(15) Delete the paragraph at page 17, lines 6-7 and insert:

*Q19* Examples of env polypeptide sequences are: SEQ ID NO:96 [HERV-K(C7)]; SEQ ID  
NO:108 [HERV-K10]; SEQ ID NO:149 ['ERV6'].

(16) Delete the paragraph at page 17, line 13 and insert:

*Q20* Examples of cORF nucleotide sequences are: SEQ ID NO:89 and SEQ ID NO:90  
[HERV-K(108)].

(17) Delete the paragraph at page 17, line 14 and insert:

Examples of cORF polypeptide sequences are SEQ ID NO:109.

A21 (18) Delete the paragraph at page 19, lines 4-8 and insert:

The invention provides an isolated polypeptide comprising: (a) an amino acid sequence selected from the group consisting of SEQ ID NOS:109 (cORF), 146 (gag), 147 (prt), 148 (pol), 149 (env); (b) a fragment of at least  $x$  amino acids of (a); or (c) a polypeptide sequence having at least  $s\%$  identity to (a). These polypeptides include variants (*e.g.* allelic variants, homologs, orthologs, mutants *etc.*).

(19) Delete the paragraph at page 19, lines 14-18 and insert:

A23 The invention also provides an isolated polypeptide having formula  $\text{NH}_2\text{-A-B-C-COOH}$ , wherein: A is a polypeptide sequence consisting of  $a$  amino acids; C is a polypeptide sequence consisting of  $c$  amino acids; B is a polypeptide sequence consisting of a fragment of  $b$  amino acids of an amino acid sequence selected from the group consisting of SEQ ID NOS:109, 146, 147, 148, 149; and said polypeptide is not a fragment of polypeptide sequence SEQ ID NO:109, 146, 147, 148 or 149.

(20) Delete the paragraph at page 19, lines 27, to page 20, line 2 and insert:

A24 The amino acid sequence of -A- typically shares less than  $n\%$  sequence identity to the  $a$  amino acids which are N-terminal of sequence -B- in SEQ ID NO:109, 146, 147, 148 or 149 and the amino acid sequence of -C- typically shares less than  $n\%$  sequence identity to the  $c$  amino acids which are C-terminal of sequence -B- in SEQ ID NO:109, 146, 147, 148 or 149. The value of  $n$  is generally 60 or less (*e.g.* 50, 40, 30, 20, 10 or less).

(21) Delete the paragraph at page 20, lines 3-8 and insert:

O25 The fragment of (b) may comprise a T-cell or, preferably, a B-cell epitope of SEQ ID NO:109, 146, 147, 148 or 149. T- and B-cell epitopes can be identified empirically (*e.g.* using the PEPSCAN method [19, 20] or similar methods), or they can be predicted (*e.g.* using the Jameson-Wolf antigenic index [21], matrix-based approaches [22], TEPITOPE [23], neural networks [24], OptiMer & EpiMer [25, 26], ADEPT [27], Tsites [28], hydrophilicity [29], antigenic index [30] or the methods disclosed in reference 31 *etc.*).

(22) Delete the paragraph at page 37, lines 10-15 and insert:

A26 The invention is based on the finding that HML-2 mRNA expression is up-regulated in

Q26  
cont. prostate tumors. Because HML-2 is a well-recognized family, the skilled person will be able to determine without difficulty whether any particular endogenous retroviruses is or is not a HML-2. Preferred members of the HML-2 family for use in accordance with the present invention are those whose proviral genome has an LTR which has at least 75% sequence identity to SEQ ID NO:150 (the LTR sequence from HML-2.HOM [1]). Example LTRs include SEQ ID NOS:151-154.

(23) Delete the paragraph at page 37, lines 20-27 and insert:

Q27 Sequences from HERV-K(CH) are shown in SEQ ID NOS:14-39 and have been deposited with the ATCC (see Table 7). The skilled person will be able to classify any further HERV as HERV-K(CH) or not based on sequence identity to these HERV-K(CH) polynucleotides. Preferably such a comparison is to one or more, or all, of the polynucleotide sequences disclosed herein or of the polynucleotide inserts in the ATCC-deposited isolates. Alternatively, the skilled artisan can determine the sequence identity based on a comparison to any one or more, or all, of the sequences in SEQ ID NOS:7-10 and SEQ ID NOS:14-39 taking into consideration the spontaneous mutation rate associated with retroviral replication. Thus, it will be apparent when the differences in the sequences are consistent with a HERV-K(CH) isolate or consistent with another HERV.

(24) Delete the paragraph at page 38, lines 7-10 and insert:

Q28 The invention provides an isolated polynucleotide comprising: (a) the nucleotide sequence of any of SEQ ID NOS:7-10; (b) the nucleotide sequence of any of SEQ ID NOS:27-39; (c) the complement of a nucleotide sequence of any of SEQ ID NOS:7-10; or (d) the complement of the nucleotide sequence of any of SEQ ID NOS:27-39.

(25) Delete the paragraph at page 38, lines 12-15 and insert:

Q29 The invention also provides an isolated polynucleotide comprising a fragment of: (a) a nucleotide sequence shown in SEQ ID NOS:7-10; (b) the nucleotide sequence shown in any of SEQ ID NOS:27-39; (c) the complement of a nucleotide sequence shown in SEQ ID NOS:7-10; or (d) the complement of the nucleotide sequence shown in any of SEQ ID NOS:27-39.

(26) Delete the paragraph at page 38, lines 22-27 and insert:

Q30 The fragment is preferably neither one of the following sequences nor a fragment of one of the following sequences: (i) the nucleotide sequence shown in SEQ ID NO:42; (ii) the



Q30  
cont nucleotide sequence shown in SEQ ID NO:43; (iii) the nucleotide sequence shown in SEQ ID NO:44; (iv) the nucleotide sequence shown in SEQ ID NO:45; (v) a known polynucleotide; or (vi) a polynucleotide known as of 7th December 2000 (e.g. a polynucleotide available in a public database such as GenBank of GeneSeq before 7th December 2000).

(27) Delete the paragraph at page 39, lines 14-17 and insert:

Q31  
~~Preferred fragments (e.g. for the identification of HERV-K(CH) polynucleotides~~  
associated with cancer) which do not correspond identically in their entirety to any portion of the sequence(s) shown in SEQ ID NOS:42-45 are: SEQ ID NO:59 (from gag region), SEQ ID NOS:60-70 (from pol region) and SEQ ID NOS:71-82 (from 3' pol region).

(28) ~~Delete the paragraph at page 39, lines 17-21 and insert:~~

Q32  
~~Preferred fragments (e.g. for the simultaneous identification of HERV-K(CH)~~  
polynucleotides, HERV-KII polynucleotides and/or HERV-K10 polynucleotides) which do correspond identically in their entirety to any portion of the sequence(s) shown in SEQ ID NOS:44 & 45 are SEQ ID NOS:83 & 84 (from gag region).

(29) Delete the paragraph at page 39, line 27, to page 40, line 9 and insert:

Q33  
The invention also provides an isolated polynucleotide comprising (a) a segment that is a fragment of the sequence shown in SEQ ID NOS:7-10 or SEQ ID NOS:27-39, wherein (i) said fragment is at least 10 nucleotides in length and (ii) corresponds identically in its entirety to a portion of SEQ ID NO:44 and/or 45; and, optionally, (b) one or more segments flanking the segment defined in (a), wherein the presence of said optional segment(s) causes said polynucleotide to not correspond identically to any portion of a sequence shown in SEQ ID NOS:7-10 or SEQ ID NOS:27-39. In some embodiments, the optional flanking segments share less than 40% sequence identity to the nucleic acid sequences shown in SEQ ID NOS:7-10, SEQ ID NO:44 and/or SEQ ID NO:45. In other embodiments, the optional flanking segments have no contiguous sequence of 10, 12, 15 or 20 nucleotides in common with SEQ ID NOS:7-10, SEQ ID NO:44 and/or SEQ ID NO:45. In yet other embodiments, the optional flanking segment is not present. In further embodiments, a fragment of the polynucleotide sequence is up to at least 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 1000, or 1500 nucleotides in length.

(30) Delete the paragraph at page 40, lines 10-19 and insert:

Q34  
The invention also provides an isolated polynucleotide having formula 5'-A-B-C-3',

7

wherein: A is a nucleotide sequence consisting of  $a$  nucleotides; B is a nucleotide sequence consisting of a fragment of  $b$  nucleotides from (i) the nucleotide sequence shown in SEQ ID NOS:7-10, (ii) the nucleotide sequence shown in any of SEQ ID NOS:27-39, (iii) the complement of the nucleotide sequence shown in SEQ ID NOS:7-10, or (iv) the complement of the nucleotide sequence shown in any of SEQ ID NOS:27-39; C is a nucleotide sequence consisting of  $c$  nucleotides; and wherein said polynucleotide is not a fragment of (i) the nucleotide sequence shown in SEQ ID NOS:7-10, (ii) the nucleotide sequence shown in any of SEQ ID NOS:27-39, (iii) the complement of the nucleotide sequence shown in SEQ ID NOS:7-10, or (iv) the complement of the nucleotide sequence shown in any of SEQ ID NOS:27-39.

A34 cont.  
(31) Delete the paragraph at page 41, lines 2-6 and insert:

The invention provides a polynucleotide having at least  $s\%$  identity to: (a) SEQ ID NOS:7-10; (b) a fragment of  $x$  nucleotides of SEQ ID NOS:7-10; (c) SEQ ID NOS:11-13; (b) a fragment of  $x$  nucleotides of SEQ ID NOS:11-13. The value of  $s$  is at least 50 (e.g. at least 55, 60, 65, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 99.5, 99.9 etc.). The value of  $x$  is at least 7 (e.g. 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100 etc.).

A35  
(32) Delete the paragraph at page 41, lines 9-14 and insert:

A36  
Variants can be identified by hybridization of putative variants with the polynucleotide sequences disclosed in SEQ ID NOS:14-39 herein, preferably by hybridization under stringent conditions. For example, by using appropriate wash conditions, variants can be identified where the allelic variant exhibits at most about 25-30% base pair (bp) mismatches relative to the selected polynucleotide probe. In general, allelic variants contain 15-25% bp mismatches, and can contain as little as even 5-15%, or 2-5%, or 1-2% bp mismatches, as well as a single bp mismatch.

(33) Delete the paragraph at page 41, line 25, to page 42, line 12 and insert:

A37  
A preferred HERV-K(CH) isolate is an isolate sequence which is shown in SEQ ID NOS:7-10. Another preferred class of HERV-K(CH) isolates are those having a nucleotide sequence identity of at least 90%, preferably at least 95% to the 3' polymerase region shown in SEQ ID NO:13 which relates to integrase, as measured by the alignment program GCG Gap (Suite Version 10.1) using the default parameters: open gap = 3 and extend gap = 1. Another

Q37 cont  
preferred class of HERV-K(CH) isolates are those having a nucleotide sequence identity of at least 98%, more preferably at least 99% to the 5' polymerase region shown in SEQ ID NO:12 which relates to reverse transcriptase, as measured by the alignment program GCG Gap (Suite Version 10.1) using the default parameters: open gap = 3 and extend gap = 1. Another typical classification of the relationship of retroviruses is based on the amino acid sequence similarities in the reverse transcriptase protein. Thus, an even more preferred class of HERV-K(CH) isolates are those having an amino acid sequence identity of at least 90%, more preferably 95% to the 5' polymerase region encoded by the nucleotide sequence shown in SEQ ID NO:12, as determined by the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 2, BLOSUM matrix of 62. Thus, these prostate cancer-associated polynucleotide sequences define a class of human endogenous retroviruses, designated herein as HERV-K(CH), whose members comprise variations which, without wanted to be bound by theory, may be due to the presence of polymorphisms or allelic variations.

---

(34) Delete the paragraph at page 42, lines 14-25 and insert:

---

Q38  
The invention provides an isolated polynucleotide comprising a polynucleotide that selectively hybridizes, relative to a known polynucleotide, to: (a) the nucleotide sequence shown in SEQ ID NOS:7-10; (b) the nucleotide sequence shown in any of SEQ ID NOS:27-39; (c) the complement of the nucleotide sequence shown in SEQ ID NOS:7-10; (d) the complement of the nucleotide sequence shown in any of SEQ ID NOS:27-39; (e) a fragment of the nucleotide sequence shown in SEQ ID NOS:7-10; (f) a fragment of the nucleotide sequence shown in any of SEQ ID NOS:27-39; (g) the complement of a fragment of the nucleotide sequence shown in SEQ ID NOS:7-10; (h) the complement of a fragment of the nucleotide sequence shown in any of SEQ ID NOS:27-39; (j) a nucleotide sequence shown in SEQ ID NOS:14-39; or (k) polynucleotides found in ATCC deposits having ATCC accession numbers given in Table 7. The fragment of (e), (f), (g) or (h) is preferably at least x nucleotides in length, wherein x is as defined in H.1.2 above, and is preferably not one of the sequences (i), (ii), (iii), (iv), (v) or (vi) as defined H.1.2 above.

---

(35) Delete the paragraph at page 43, lines 2-7 and insert:

---

Q39  
The invention also provides an isolated polynucleotide comprising: (a) a HERV-K(CH) cDNA insert as deposited at the ATCC and having an ATCC accession number given in Table 7;

A39  
cont (b) a HERV-K(CH) sequence as shown in any one of SEQ ID NOS:14-26; (c) a HERV-K(CH) sequence as shown in any one of SEQ ID NOS:27-39; or (d) a fragment of (a), (b) or (c). The fragment of (d) is preferably at least  $x$  nucleotides in length, wherein  $x$  is at least 7 (e.g. at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100 etc.).

43  
(36) Delete the paragraph at page 41, lines 9-22 and insert:

A40 Preferred polynucleotides of the invention are those having a sequence set forth in any one of the polynucleotide sequences SEQ ID NOS:7-10 and SEQ ID NOS:14-39 provided herein; polynucleotides obtained from the biological materials described herein, in particular, polynucleotide sequences present in the isolates deposited with the ATCC and having ATCC accession numbers given in Table 7 or other biological sources (particularly human sources) or by hybridization to the above mentioned sequences under stringent conditions (particularly conditions of high stringency); genes corresponding to the provided polynucleotides; variants of the provided polynucleotides and their corresponding genes particularly those variants that retain a biological activity of the encoded gene product (e.g. a biological activity ascribed to a gene product corresponding to the provided polynucleotides as a result of the assignment of the gene product to a protein family(ies) and/or identification of a functional domain present in the gene product). Other polynucleotides and polynucleotide compositions contemplated by and within the scope of the present invention will be readily apparent to one of ordinary skill in the art when provided with the disclosure here.

(37) Delete the paragraph at page 45, lines 9-11 and insert:

A41 The invention provides an isolated polypeptide: (a) encoded within a HERV-K(CH) open reading frame; (b) encoded by a polynucleotide shown in SEQ ID NO:11, 12 or 13; or (c) comprising an amino acid sequence as shown in any one of SEQ ID NOS:46-49, 50-55, 56-57 or 58.

(38) Delete the paragraph at page 45, lines 12-18 and insert:

A42 Deduced polypeptides encoded by the HERV-K(CH) polynucleotides of the invention include the gag translations shown in SEQ IDS 46-49 and the 3' pol translations shown in SEQ ID NOS:50-55. A polypeptide sequence encoded by the polynucleotide having the sequence shown in SEQ ID NO:15 is provided in SEQ ID NO:56; a polypeptide sequence encoded by the

Q42  
cont  
polynucleotide having the sequence shown in SEQ ID NO:14, is shown in SEQ ID NO:57. A consensus 3' pol polypeptide sequence encoded by the polynucleotides having the sequence shown in SEQ ID NOS:21-27, inclusive, is provided in SEQ ID NO:58.

(39) Delete the paragraph at page 45, lines 19-25 and insert:

Q43  
The polypeptides encompassed by the present invention include those encoded by polynucleotides of the invention, e.g. SEQ ID NOS:7-10 and SEQ ID NOS:14-39, as well as polynucleotides deposited with the ATCC as disclosed herein, as well as nucleic acids that, by virtue of the degeneracy of the genetic code, are not identical in sequence to the disclosed polynucleotides and encode the polypeptides. Thus, the invention includes within its scope a polypeptide encoded by a polynucleotide having the sequence of any one of the polynucleotide sequences provided herein, or a variant thereof.

(40) Delete the paragraph at page 46, lines 17-20 and insert:

Q44  
The invention provides an isolated polypeptide comprising a fragment of: (a) a polypeptide sequence encoded within a HERV-K(CH) open reading frame; (b) a polypeptide sequence encoded by a polynucleotide shown in SEQ ID NO:11, 12 or 13; or (c) an amino acid sequence as shown in any one of SEQ ID NOS:46-49, 50-55, 56-57 or 58.

(41) Delete the paragraph at page 46, lines 25-26 and insert:

Q45  
The fragment may include an epitope e.g. an epitope of the amino acid sequence shown in SEQ ID NOS:56, 57 or 58.

(42) Delete the paragraph at page 46, line 27, to page 47, line 10 and insert:

Q46  
SEQ ID NOS:46-49 provide a translation of the HERV-K(CH) polynucleotides having a sequence shown in SEQ ID NOS:14, 15, 16 and 40 (the sequence of SEQ ID NO:40 is from a polynucleotide found in a normal prostate library) corresponding to polynucleotides encoding the gag region. SEQ ID NOS:50-55 provide a translation of the HERV-K(CH) polynucleotides having a sequence shown in SEQ ID NOS:21-26, inclusive, corresponding to the 3' region of pol. SEQ ID NOS:56 & 57 provide translations of the HERV-K(CH) polynucleotide of SEQ ID NO:15 and SEQ ID NO:14, respectively. SEQ ID NO:58 provides a consensus translation of the polynucleotide from the 3' pol region (SEQ ID NOS:21-26, inclusive). Encompassed with the present invention are polypeptide fragments, such as, epitopes, of at least 5 amino acids, at least 6 amino acids, at least 8 amino acids, at least 10 amino acids, at least 11 amino acids, at least

A46  
cont. amino acids, at least 13 amino acids, at least 14 amino acids and at least 15 amino acids of the translations shown in SEQ ID NOS:46-49 and 50-55. In a preferred embodiment, the HERV-K(CH) epitopes of the amino acid sequence as shown in SEQ ID NOS:56-58 were determined by the Jameson-Wolf antigenic index [21].

(43) Delete the paragraph at page 47, lines 11-18 and insert:

A47  
The following regions in 3' pol (SEQ ID NO:58) were determined to be antigenic by Jameson-Wolf algorithm: amino acids: 1-10; 15-35; 45-55; 60-85; 100-115; 125-140; 170-190; 195-215; 230-268. Additional epitope-containing fragments include amino acids 1-8; 2-10; 1-15; 5-15; 7-15; 10-20; 12-20; 15-23; 20-28; 28-35; 15-30; 15-40; 20-30; 45-52; 48-55; 60-68; 60-70; 65-73; 70-78; 75-83; 70-80; 65-75; 68-75; 75-85; 78-85; 65-85; 60-75; 100-108; 103-110; 105-113; 108-115; 125-133; 128-135; 132-140; 170-178; 175-182; 180-187; 182-190; 195-202; 200-208; 205-212; 208-215; 230-237; 235-242; 240-247; 245-252; 250-257; 255-262; 260-268; 230-250; 235-255; 240-260; 245-268; 230-245; 235-245; 235-250; 240-255; 245-260; 250-268; 15-55; 170-215; 45-85.

(44) Delete the paragraph at page 47, lines 19-27 and insert:

A48  
The following regions in gag (SEQ ID NO:56) were determined to be antigenic by Jameson-Wolf algorithm: amino acids: 1-40; 45-60; 80-105; 130-145; 147-183; 186-220; 245-253; 255-288. Additional epitope-containing fragments include amino acids 1-8; 2-10; 1-15; 5-15; 7-15; 10-20; 12-20; 15-23; 20-28; 28-35; 30-37; 33-40; 1-20; 20-40; 1-15; 15-30; 15-40; 45-52; 50-57; 55-62; 50-60; 1-60; 80-87; 85-92; 80-90; 90-97; 95-102; 98-105; 85-100; 90-105; 80-100; 85-105; 130-137; 135-142; 140-147; 145-152; 150-157; 155-162; 160-167; 165-172; 170-177; 175-183; 180-187; 185-192; 190-197; 195-202; 200-207; 205-212; 210-217; 213-220; 185-220; 190-220; 195-220; 200-220; 205-220; 255-262; 260-267; 265-272; 270-277; 275-282; 280-288; 245-288; 250-288; 260-288; 265-288; 270-288.

(45) Delete the paragraph at page 47, line 28, to page 48, line 9 and insert:

A49  
The following regions in gag (SEQ ID NO:57) were determined to be antigenic by Jameson-Wolf algorithm: amino acids: 1-40; 80-105; 145-180; 185-225; 240-335. Additional epitope-containing fragments include amino acids 1-8; 2-10; 1-15; 5-15; 7-15; 10-20; 12-20; 15-23; 20-28; 28-35; 30-37; 33-40; 1-20; 20-40; 1-15; 15-30; 15-40; 80-87; 85-92; 80-90; 90-97; 95-102; 98-105; 85-100; 90-105; 80-100; 85-105; 145-152; 150-157; 155-162; 160-167; 165-

172; 170-177; 175-182; 180-187; 185-192; 190-197; 195-202; 200-207; 205-212; 210-217; 215-212; 218-225; 145-160; 150-165; 155-170; 160-175; 170-185; 180-225; 185-225; 190-225; 195-225; 200-225; 205-225; 210-225; 215-225; 240-247; 245-252; 250-257; 255-262; 260-267; 265-272; 270-277; 275-282; 280-287; 285-292; 290-297; 295-302; 300-307; 305-312; 310-317; 315-322; 320-327; 325-332; 328-335; 245-285; 250-285; 260-285; 265-285; 270-295; 275-300; 280-305; 285-310; 295-315; 300-320; 305-325; 325-335; 245-335; 250-335; 255-335; 260-335; 270-335; 275-335; 280-335; 285-335; 290-335; 295-335; 305-335; 310-335; 315-335; 320-335.

A49  
Concl

(46) Delete the paragraph at page 48, lines 11-16 and insert:

A50

The invention also provides an isolated polypeptide having formula 5'-A-B-C-3', wherein: A is an amino acid sequence consisting of *a* amino acids; B is an amino acid sequence consisting of a fragment of *b* amino acids from (i) the amino acid sequence encoded by a polynucleotide shown in SEQ ID NO:11, 12 or 13; (ii) any one of SEQ ID NOS:46-49, 50-55, 56-57 or 58; C is an amino acid sequence consisting of *c* amino acids; and wherein said polypeptide is not a fragment of the amino acid sequence defined in (i) or (ii).

(47) Delete the paragraph at page 48, line 25, to page 49, line 2 and insert:

A51

The invention provides a polypeptide having at least *s*% identity to: (a) the polypeptide sequences encoded by SEQ ID NOS:7-45; (b) a fragment of *x* amino acids of the polypeptide sequences encoded by SEQ ID NOS:7-45; (c) the polypeptide sequences SEQ ID NOS:46-58; (d) a fragment of *x* amino acids of the polypeptide sequences SEQ ID NOS:46-58. The value of *s* is at least 35 (e.g. at least 40, 45, 50, 55, 60, 65, 70, 75, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 99.5, 99.9 etc.). The value of *x* is at least 7 (e.g. 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100).

(48) Delete the paragraph at page 49, lines 13-20 and insert:

A52

The invention provides polypeptides, such as those shown in SEQ ID NOS:46-58, encoded by HERV-K(CH) polynucleotides that are differentially expressed in prostate cancer cells. Such polypeptides are referred to herein as "polypeptides associated with prostate cancer" or "HERV-K(CH) polypeptides". The polypeptides can be used to generate antibodies specific for a polypeptide associated with prostate cancer, which antibodies are in turn useful in diagnostic methods, prognostic methods, therametric methods, and the like as discussed in more

Q52  
C501 detail herein. Polypeptides are also useful as targets for therapeutic intervention, as discussed in more detail herein.

(49) Delete the paragraph at page 49, line 27, to page 50, line 5 and insert:

Q53 Polypeptides, such as polypeptides of the gag regions or polypeptides of the pol regions, encoded by the polynucleotides disclosed herein, such as polynucleotides having the sequences as shown in SEQ ID NOS:7-10 and SEQ ID NOS:14-39, and in isolates deposited with the ATCC and having ATCC accession numbers given in Table 7 and/or their corresponding full length genes, can be used to screen peptide libraries to identify binding partners, such as receptors, from among the encoded polypeptides. Peptide libraries can be synthesized according to methods known in the art (*e.g.* see refs. & ).

(50) Delete the paragraph at page 58, lines 15-24 and insert:

Q54 In one preferred embodiment of the present invention, an array comprises at least two polynucleotides, each having a sequence selected from the group consisting of SEQ ID NOS:14-39 and polynucleotides present in isolates deposited with the ATCC and having ATCC accession numbers PTA-2561, PTA-2572, PTA-2566, PTA-2571, PTA-2562, PTA-2573, PTA-2560, PTA-2565, PTA-2568, PTA-2564, PTA-2569, PTA-2567, PTA-2559, PTA-2563, PTA-2570. In another preferred embodiment, an array comprises at least one polynucleotide having a sequence selected from the group consisting of SEQ ID NOS:14-39 and polynucleotides present in isolates deposited with the ATCC and having ATCC accession numbers PTA-2561, PTA-2572, PTA-2566, PTA-2571, PTA-2562, PTA-2573, PTA-2560, PTA-2565, PTA-2568, PTA-2564, PTA-2569, PTA-2567, PTA-2559, PTA-2563, PTA-2570 and at least one of a polynucleotide having a sequence shown in SEQ ID NO:42 or 43.

(51) Delete the paragraph at page 64, lines 5-19 and insert:

Q55 This invention also provides methods for detecting cancer associated with elevated levels of HERV-K(CH) polynucleotides, in particular in prostate cancer, by means of (i) detecting polynucleotides having at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or at least 100% identity to the polynucleotide shown in SEQ ID NOS:7-10 or to polynucleotides in isolates deposited with the ATCC and having ATCC deposit accession numbers PTA-2561, PTA-2572, PTA-2566, PTA-2571, PTA-2562, PTA-2573,



PTA-2560, PTA-2565, PTA-2568, PTA-2564, PTA-2569, PTA-2567, PTA-2559, PTA-2563, PTA-2570, as measured by the alignment program GCG Gap (Suite Version 10.1) using the default parameters: open gap = 3 and extend gap = 1 or polynucleotides hybridizing under high stringency conditions to the polynucleotide shown in SEQ ID NOS:7-10; (ii) detecting polypeptides, or fragments thereof encoded by the sequences of (i); and (iii) detecting antibodies specific for one or more of the polypeptides. Furthermore, (iv) detecting particles associated with overexpression of HERV-K(CH) polynucleotides may also be used in the diagnosis of cancer, in particular, prostate cancer, and monitoring its progression.

*A55 cont.*  
(52) Delete the paragraph at page 65, lines 17-22 and insert:

*A56*  
Accordingly, the present invention provides kits for detecting prostate cancer comprising at least one of polynucleotides having the sequence as shown in SEQ ID NOS:7-10, SEQ ID NOS:14-39, or fragments thereof, or having the sequence found in an isolate deposited with the ATCC and having ATCC accession numbers PTA-2561, PTA-2572, PTA-2566, PTA-2571, PTA-2562, PTA-2573, PTA-2560, PTA-2565, PTA-2568, PTA-2564, PTA-2569, PTA-2567, PTA-2559, PTA-2563, PTA-2570 or fragments thereof.

(53) Delete the paragraph at page 68, lines 1-13 and insert:

*A57*  
Polynucleotide generally comprising at least 10 nt, at least 12nt or at least 15 contiguous nucleotides of a polynucleotide provided herein, such as, for example, those having the sequence as depicted in SEQ ID NOS:7-10, and 3-28, are used for a variety of purposes, such as probes for detection of and/or measurement of, transcription levels of a polynucleotide that is differentially expressed in a prostate cancer cell. A probe that hybridizes specifically to a polynucleotide disclosed herein should provide a detection signal at least 5-, 10-, or 20-fold higher than the background hybridization provided with other unrelated sequences. It should be noted that "probe" as used herein is meant to refer to a polynucleotide sequence used to detect a differentially expressed gene product in a test sample. As will be readily appreciated by the ordinarily skilled artisan, the probe can be detectably labeled and contacted with, for example, an array comprising immobilized polynucleotides obtained from a test sample (e.g. mRNA). Alternatively, the probe can be immobilized on an array and the test sample detectably labeled. These and other variations of the methods of the invention are well within the skill in the art and are within the scope of the invention.

(54) Delete the paragraph at page 71, lines 20-23 and insert:

Figure 6 shows an alignment of env genomic DNA sequences from 27 HERV-K viruses. A consensus sequence (SEQ ID NO:157) is shown on the bottom line.

Q58 Figures 7-9 show alignments of inferred polypeptide sequences for gag (7), pol (8) and env (9) from various HERV-K viruses, together with consensus sequences (SEQ ID NOS:158-160).

(55) Delete the paragraph at page 77, lines 4-12 and insert:

Q59 The 16 isolates were initially determined in a first pass sequencing reaction to have the sequences as shown in SEQ ID NOS:27-39, inclusive. The isolate from the normal prostate tissue was initially determined in a first pass sequencing reaction to have the sequence as shown in SEQ ID NO:41. A first pass sequencing reaction refers to a high-throughput process, where PCR reactions generate the sequencing template then sequencing is performed with one of the PCR primers, in a single direction. A search of public databases revealed that these 16 isolates have some degree of identity to regions of the human endogenous retrovirus HERV-K(II) sequence disclosed in Genbank accession number AB047240 and shown in SEQ ID NO:44, and also to HERV-K(10), but are nonetheless unique.

(56) Delete the paragraph at page 77, lines 13-19 and insert:

Q60 The isolates were subjected to a second round of nucleic acid sequencing and were found to have the sequences as shown in SEQ ID NOS:14-26, inclusive. The isolate from the normal prostate tissue was subjected to a second round of nucleic acid sequencing and found to have the sequence as shown in SEQ ID NO:40. This second round of sequencing is a customized process, where sequencing is performed on purified dsDNA template in a DNA vector. Sequencing is done from both ends of the template, forward and reverse, with primers designed from the flanking regions of the vector, and new primers are synthesized for every additional reaction needed to span the entire insert.

(57) Delete the paragraph at page 77, line 28, to page 78, line 8 and insert:

Q61 Composite HERV-K(CH) polynucleotide sequences are shown in SEQ ID NOS:7, 8, 9 and 10 and Figure 1 provides a schematic illustration of a human endogenous retrovirus and the HERV-K(CH) species within the schematic illustration. SEQ ID NO:7 is a composite sequence of the polynucleotides SEQ ID NOS:14-16, inclusive, and has a consensus sequence as shown in

Q61  
cont. SEQ ID NO:11. This region corresponds to the gag region of a human endogenous retrovirus. SEQ ID NOS:8 and 9 are composite sequence of the polynucleotides having a sequence as shown in SEQ ID NOS:17-20, inclusive, and has a consensus sequence as shown in SEQ ID NO:12. This region corresponds to the 5' pol region of a human endogenous retrovirus. SEQ ID NO:10 is a composite sequence of the polynucleotides having a sequence as shown in SEQ ID NOS:21-26, inclusive, and has a consensus sequence as shown in SEQ ID NO:13. This region corresponds to the 3' pol region of a human endogenous retrovirus.

(58) Delete the paragraph at page 78, lines 18-23 and insert:

Q62 Consensus polynucleotide sequences SEQ ID NOS:11-13 were generated with Multiple Sequence Alignment (MSA), a web implementation of the GCG Pileup and Pretty programs. The program uses a clustering algorithm similar to the Clustal program described in reference . The default values for the alignments and consensus extraction were 8 for gap open and 2 for gap extension. The poling plurality or minimum number of like sequences specified to assign a residue to the consensus sequence was 2.

(59) Delete the paragraph at page 78, lines 24-29 and insert:

Q63 The polynucleotide sequences shown in SEQ ID NOS:14-16, inclusive, were used for the consensus polynucleotide sequence shown in SEQ ID NO:11. The polynucleotide sequences shown in SEQ ID NOS:17-20, inclusive, were used for the consensus polynucleotide sequence shown in SEQ ID NO:12. The polynucleotide sequences shown in SEQ ID NOS:21-26, inclusive, were used for the consensus polynucleotide shown in SEQ ID NO:13. The "N" represents where there is no qualifying minimum representative base. i.e. at least two sequences with the same base at that site.

(60) Delete the paragraph at page 79, lines 1-5 and insert:

Q64 Northern blotting of prostate cancer cell lines using nucleotides 243-end of SEQ ID NO:150 labeled as a probe indicates that they express PCAV transcripts of several sizes, corresponding to both full-length viral genomic sequences and to sub-genomic spliced transcripts (Figure 5). Expression of such transcripts have also been observed in teratocarcinoma cell lines [15], as shown in lane 1 of figure 14.